Atopic dermatitis. Interdisciplinary diagnostic and therapeutic recommendations of the Polish Dermatological Society, Polish Society of Allergology, Polish Pediatric Society and Polish Society of Family Medicine. Part I. Prophylaxis, topical treatment and phototherapy

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Abstract

Atopic dermatitis is a chronic and recurrent inflammatory dermatosis with concomitant intensive pruritus, and is diagnosed both in children and adults. Atopic dermatitis-patients are predisposed to have bacterial, viral and fungal skin infections; they also suffer from an increased risk of developing food allergies (especially, at an infantile age), allergic rhinitis, or bronchial asthma (a so-called atopic march). Currently, an increasing atopic dermatitis incidence constitutes a serious medical problem that regards not only dermatology and allergology, but also paediatrics, and family medicine. The basis for atopic dermatitis treatment and prophylaxis is restoration of epidermal barrier functions by means of tailored emollients. Atopic dermatitis therapies should effectively eliminate clinical symptoms of the disease, prevent exacerbations as well as complications, and improve patients' quality of life.

Key words: atopic dermatitis, allergic march, elimination diet, emollients, topical glucocorticoids, topical calcineurin inhibitors, proactive therapy, wet dressings therapy, wet dressings.

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Introduction

Atopic dermatitis

Atopic dermatitis (AD) is a common chronic recurrent non-infectious inflammatory disease that most often appears in early childhood and may persist for life. The disease is characterized by periods or exacerbations and remissions. The main symptoms include: intense pruritus and skin dryness, erythematous inflammatory skin lesions with eczematous morphology; chronic phase of the disease involves thickening (lichenization) and exfoliation of the epidermis. Patients tend to suffer from recurrent bacterial, viral and fungal skin infections. The lesions are most often form on the bends of elbows and knees, on the face and neck, but they may also cover the skin of the entire body (erythroderma). The site of exanthemata is age-related. Atopic dermatitis is a result of complex genetic, epigenetic, environmental and immunological interactions with a concomitant epidermal barrier defect [1, 2].

During the first years of life, AD incidence is similar in both sexes; after the age of 6, prevalence of the female sex over male is noted (3 : 2) [3, 4]. Atopic dermatitis usually starts in early childhood. It is believed that in 45% of infants symptoms appear before the 6th month of life, and in 50% before they are 1 y/o. In 40–80% of children the disease tends to recede before the age of 5, and in 20% of patients it is present till adulthood. In one out of four adult AD-patients, the disease develops *de novo* [5, 6]. Large cities in Poland have been experiencing an increase in AD incidence. The AD incidence percentage among children ranges from 4.7 to 9.2%, and among adults from 0.9% to 1.4% [7].

Chronic course of the disease and continual pruritus significantly decrease the quality of life of patients and their families, and lead to serious socio-economic consequences. Sleep disorders, absence at school and work, and social isolation may be the reasons behind depression, and even suicidal thoughts.

Allergic march

Atopic dermatitis may be concomitant with other IgE-dependent atopic diseases: bronchial asthma, allergic upper respiratory congestion and catarrhal conjunctivitis, and sometimes even food allergies. Epidemiological studies and clinical observations indicate the existence of a specific sequence of occurrence of atopic diseases. This phenomenon was called an allergic march and does not always have a classic course. About 34% of AD-patients develop allergic rhinitis, 20–35% – asthma, and 15% – clinical symptoms of food allergies. Genetic factors and external factors such as stress, eating habits, infections, cigarette smoke, or smog, mainly predispose individuals to develop an allergic disease and allergic march [1, 2].

Treatment – general recommendations

An increase in AD incidence constitutes a serious medical and therapeutic problem that regards not only dermatology and allergology, but also paediatrics and family medicine [1, 2, 8–10]. While commencing the AD treatment, not only should patient's age and site of skin lesions be taken into account, but also intensity of the inflammation (Table 1), and concomitant diseases, including: infections, contact allergy, food allergy, eye diseases, mental diseases, obesity, and cardiovascular diseases [8–10]. Contact eczema is confirmed in about 50% of children with initial diagnosis of AD [11, 12].

Special scales are used to objectively measure the intensity of skin lesions in AD [13]. SCORAD (Scoring Atopic Dermatitis) has been recognized to be the most reliable tool to measure clinical symptoms of AD – together with EASI (Eczema Area and Severity Index) [13, 14]. SCORAD allows for assessing the area of involved skin, and the intensity of particular skin symptoms (dryness, erythema, oedema, effusion, erosions, lichenization) on a point scale from 0 to 3. Moreover, SCORAD includes the assessment of subjective symptoms: sleep disorders and pruritus intensity from 0 to 10; the assessment is provided by the patient. It is available for physicians as a computer or smartphone application. The scale facilitates treatment monitoring and objectivizing treatment results. The PO-SCORAD (Patient-Oriented Scoring Atopic Dermatitis) version based on SCORAD was created for patients. It correlates well with SCORAD, and correlates better with other scales that assess quality of life (e.g. DLQI) [13, 15]. It is available as a convenient computer or smartphone application (https://www.poscorad.com/#/poscorad/pl). The application allows patients to assess the intensity of the disease themselves, and track its intensity; it also reminds the patients to use emollients, and sends information to physicians during the period between appointments. By introducing elements of self-assessment, treatments are more effective and less costly, while patients' quality of life is improving [16].

EASI scale allows for assessing intensity of lesions from 0 to 3. The scale does not include subjective symptoms. It is mainly used in clinical studies. Other, less common scales that assess intensity of lesions in AD are POEM (Patient-Oriented Eczema Measure) and IGA (Investigators' Global Assessment) [15].

The basis for AD treatment is a combination of everyday emollient therapy that restores epidermal barrier functions and anti-inflammatory treatment with simultaneous avoidance of contact with allergens and irritating factors (Tables 1 and 2). During periods of disease exacerbations, possible concomitant bacterial, viral or fungal infections should be taken into account, and proper antimicrobial treatment should be applied. If the topical therapy fails to bring improvements, it is recommended to commence phototherapy or systemic treatment [17–19].

Table 1. Atopic dermatitis (AD) therapy depending on the intensity of the disease according to SCORAD [17–19] (the next steps in the table complement previous treatment)

Severe AD SCORAD > 50	Hospitalization
	Cyclosporine A (CyA)
	Dupilumab
	Methotrexate (MTX), mycophenolate mofetil (MMF)
	Azathioprine (AZA)
	Oral GCs (maximum for 7 days)
Moderate AD SCORAD 25–50	Wet dressings
	Climate therapy
	Psychological/psychiatric interventions
	Phototherapy: UVB 311, UVA 1, PUVA (adults)
	Proactive therapy
Mild AD SCORAD < 25	Antiseptics
	Topical calcineurin inhibitors
	Topical glucocorticosteroids (topical GCs)
Primary therapy	Emollient therap
	Avoid clinically significant allergens
	EDUCATION

Table 2. Primary AD therapy

Emollient therapy	Direct application of emollients on the inflammation is tolerated badly
	It is best to use anti-inflammatory drugs (topical GCs, topical calcineurin inhibitors)
	Apply at least 2–3 times a day!
	Glycerol is better tolerated than urea and sodium chloride
	Propylene glycol causes irritation easily and should not be used
	It is recommended to use emollients without protein allergens and haptens
Skin cleaning	Gently and thoroughly; mechanically
	Cleaning substances with/without aseptic substances
	Proper galenic forms
	Physiological pH within the 5.5–6 range
	Fast baths ≤ 5 min, temp. 27–30°C
	Adding to the bath 1/2 glass of sodium hypochlorite eliminates pruritus
Education	Apply proper amounts of emollients (250–500 g/week)
	Explain/demonstrate how to use them
	When using different topical drugs, keep a time gap
	At least once a year remind about the recommendations!

Primary therapy

Education

Lack of co-operation from the patient's side and/or caretaker's is a common reason behind therapy's failure, and thus, educational programs, "schools of atopy", informational leaflets, films, etc. are necessary and significant parts of the treatment. The patient and/or their caretaker should actively participate in the treatment process and have sufficient amount of information regarding the disease. When patients understand the necessity of continual long-term and often multi-specialist treatment, the efficacy is much improved [20–30].

Prophylaxis

Primary prophylaxis – regards children in the risk group that do not have any disease symptoms. Its aim is to prevent the disease development. Activities associated with primary prophylaxis include prolonged breastfeeding, refraining from smoking during pregnancy, limiting exposure to airborne allergens, mainly dust mites, and application of emollients from the first day of life. Both in children with population risk and in high-risk groups, it is recommended to breastfeed exclusively until the 4–6 month of life. Breastfeeding allows for limiting the adverse reactions to protein from other species. Moreover, human milk satisfies all nutritional needs, it is a natural and the most balanced food; it contains a number of biologically active substances with immunological value, among others.

Secondary prophylaxis – regards patients, in whom early symptoms of the disease were confirmed. Its aim is to prevent the appearance or exacerbation of symptoms. Emollient therapy (every 4–6 h), avoidance of irritating factors and stress, as well as elimination of allergens responsible for the symptom appearance are recommended. An important part of this prophylaxis types is vocational guidance service.

Tertiary prophylaxis – recommended in patients with full-blown AD in order to decrease the intensity of symptoms and frequency of their recurrence, and to prevent the development of concomitant diseases. This type of prophylaxis includes psychological counselling, and education of patients in order to teach them how to control the symptoms and live with the disease [31].

While taking patient's history, factors that potentially intensify the clinical symptoms should be looked for. Most frequently these include: exposure to airborne and contact allergens, food, various environmental irritating factors (including cigarette smoke and microorganisms), climate factors, stress, and disorders of the hormonal balance [17, 18, 32]. Not every AD-patient reacts to all of

Table 3. Diagnostics of food allergies in patients with moderate or severe AD, in whom symptoms persist despite general treatment and topical therapies [35, 38]

Age	Tests
< 5 y/o	Cow milk, eggs, wheat, soya, and peanuts
> 5 y/o	Choosing food for tests should be done according to the patient's history and most common allergies in this population: nuts, shellfish, fish
Youths, older age groups	Concomitant pollen and food allergy should be taken into account: apples, celeries, carrots, hazelnuts

the abovementioned factors. Hypersensitivity to airborne allergens regards most often older children and youths as well as adults [33]. Prophylaxis includes avoidance of clinically significant allergens for a given patients, i.e. pollen (from trees, shrubs, grasses, weeds, grains) during pollination time, allergens associated with dust mites, and contact allergens in case of positive test results and their connection to clinical symptoms [18]. Room ventilation and spending less time in closed spaces are important parts of the therapy.

Elimination diet

Elimination diet in recommended in patients to determine the etiopathogenetic connections between food intolerance and AD (Table 3) [34]. Eliminating harmful food from patient's diet together with proper pharmacological treatment successfully helps to achieve satisfactory clinical improvements and accelerate the treatment process [33, 35–38]. Individual recommendations with regard to eliminating chosen food from the diet regard only those patients, in whom a negative influence of food intolerance on clinical course of the primary disease was confirmed in an objective way [35].

Elimination diet in AD-patients with concomitant hypersensitivity to food intolerance

Food that contains harmful allergens needs to be temporarily eliminated from the diet of an AD-patient, and substituted with other non-allergic components with balanced or similar nutritional characteristics [39]. The elimination usually involves one or two nutritionally bivalent foods (most often: cow milk and milk products, eggs, soya, crop plants, fish, and some fruit as well as vegetables).

Validity criteria of the elimination diet are determined by: confirmed concomitant food intolerance and therapeutic efficacy of the diet (remission of skin symptoms or their total remission, minimization of exacerbation and recurrence episodes). Due to the lack of guidelines as to the duration of elimination of harmful food from the diet, the duration needs to be set individually for every patient. When the elimination diet needs to be used long-term, at least once a year a challenge test with the harmful food should be performed on the patient. The test aims at assessing the activity of the food intolerance process. A systematic decrease in this activity is a sign of an AD-patient acquiring immunological tolerance. The process, colloquially called "growing out of a food allergy", results from the used dietetic and pharmacological treatment [39].

In case of severe AD involving a multifood/polyvalent allergy, it may be necessary to eliminate even a couple of foods simultaneously from the sick child's diet. Elimination diet recommended to such patients should be balanced, what is of key importance especially for patients at the developmental age [39, 40].

Patients with multifood allergies

Patients with multifood allergies that are hypersensitive to both cow milk proteins and milk substitute products and some other products than milk constitute a special subgroup of AD-patients. Such patients are introduced to basic formulas that substitute milk in order to balance their diet. They are totally non-allergic to the patient's organism since native protein fraction of cow mild has been substituted with a pool of synthetic amino acids [41].

In case of an infant with AD characterized by moderate-severe and severe course that is fed naturally and in whom appearance of skin lesions has a confirmed causal relation to mother's eating habits, there are indications for temporary elimination of some foods from her diet. In most cases the elimination regards milk and milk products, eggs, earthnuts, nuts, some fruit and vegetables. Composition of the mother's elimination diet and its duration should be supervised by a physician or dietician. It should be remembered that the menu of the breastfeeding mother who uses elimination diet should be enriched with 500 kcal/day, include a substitute of another protein than the one eliminated from the diet, and supplemented with necessary intake of mineral salts (including 1 g Ca^{++}/day) and vitamins [41].

If a breastfeeding mother is on elimination diet an the condition of her infant fails to improve within 2 weeks, further food elimination needs to be discontinued.

If an infant who is breastfed experiences an anaphylactic reaction that is associated with its mother eating food that allergizes the infant (e.g. milk, eggs, fish, earthnuts), it is an indication to discontinue breastfeeding immediately and give the infant a formula that substitutes milk. Such formulas contain hydrolysed casein fraction or whey protein, and have a decreased ability to allergize as compared with native protein fractions of cow milk [41].

Emollient therapy

Prophylactic activities include also emollient therapy as it has been confirmed that using it since the birth of

a child that belongs to an AD risk group significantly decreases the risk of developing AD. Emollients applied from the first day of life in children born in atopic families decrease the risk of developing AD by half [42–44]. A role of emollients in inhibiting the development of allergic march and their common application in prophylaxis for AD group risks and general population is being examined [44–48].

Emollients contain occlusive substances (petroleum jelly, paraffin, mineral oils) that decrease transepidermal water loss (TEWL), moisturizing substances – water-binding humectants (e.g. urea, sorbitol, glyceryl alcohol, lactic acid), and lipids that seal the epidermal barrier (ceramides, cholesterol, polyenic acids) [49, 50]. Emollients reduce clinical symptoms of AD in children and adults, while preventing exacerbations and recurrence of atopic eczema, maintain remission state after its induction with topical anti-inflammatory preparations, and visibly decreasing the amount of used topical GCs (steroid sparing effects) [51–62].

It is recommended to use emollients 2–3 times a day in the amount of minimum 200 g/week in small children and 500 g/week in adults [18, 26]. They should be chosen individually depending on the level of skin dryness, activity during the day and night, and a possible contact allergy. Since some emollients contain ingredients with a variable allergizing potential, it is necessary to read about their composition before use [63]. Applied emollients should not contain heptens that cause contact allergies (odoriferous substances, including essential oils, preservatives such as methylisothiazolinone, and lanoline/wool alcohol), and potentially allergizing proteins, especially in the group of patients who are under the age of 2 [18]. The risk for developing a secondary contact allergy to skin care products and drugs used externally in AD treatment is the highest in severe cases of this disease [64]. It is not recommended to use pure oil, e.g. coconut, as it dries the skin and intensified TEWL. Propylene glycol should not be used in children under 2, because it can easily irritate gentle epidermis of a child [18]. Due to the fact the urea may cause skin irritation or burning sensation, its concentration in emollients for children and youths should be lower than in preparations used by adults [65].

Currently, it is recommended to use emollients plus enriched with additional active substances such as flavonoids, saponins, or bacterial lysates with *Aquaphilus dolomiae*, *Vitreoscilla filiformis*. They show anti-inflammatory effects by inhibiting cytokines (TSLP, IL-18, IL-2, IL-12, IL-17, IFN-γ, IL-1β, TNF-α, IL-4) and chemokines (MCP3/CCL7, MDC/CCL22, MIP-3a/CCL20) [18, 38], antipruritic effects [66], they support congenital immunity by activating TLR2, TLR4, TLR5, and natural anti-bacterial peptides (hBD-2, cathelicidin LL-37, psoriasin) [67], inhibit the growth of *Staphylococcus aureus*, and do not disturb the composition of bacterial flora; they also restore homeostasis of skin microbiome in AD [68, 69], and reconstruct the epidermal barrier.

Opened emollient containers need to be stored at refrigerators; it is recommended to use containers with pumps or a lid that ensures sterility, to avoid direct application of the preparation with hands, and not to share the ointment with others as the risk of contamination with microorganisms increases [18, 19].

Atopic skin requires special care processes (Table 3). Short baths with the use of preparations substituting soap and emollient therapy immediately after the bath (within 3 min) are recommended [18, 19].

In case of inflammation, topical anti-inflammatory therapy should be applied first, as even the best emollients may irritate the inflamed skin, and discourage the patients from their further use [18].

Topical anti-inflammatory therapy

Topical glucocorticosteroids

Topical glucocorticosteroids (topical GCs) have constituted the basis for AD treatment for over 50 years. Together with emollients they ensure excellent therapeutic effects. Due to skin dryness, topical GCs in the form of ointment are preferred, except for oozing lesions – in the case of these lighter forms should be applied (lotion, aerosol, cream). Application of topical GCs decreases skin colonization with *S. aureus*. During exacerbation periods, it is recommended to use topical GCs with a moderate effect in the evening, because they also have anti-pruritic qualities apart from providing anti-inflammatory effects [17–19].

Due to high efficacy obtained within a short time since the therapy introduction and low price, topical GCs are often abused. In children, these drugs should be used carefully and under close dermatological supervision, because children have a different skin structure. The choice of a preparation should be associated with disease intensity, site of lesions, age of the patients, medium in which the active substance is suspended, and drug registration (Table 4). According to the Summary Product Characteristics (SPC), fluticasone propionate, alclometasone, and betamethasone valerate are allowed for patients above the age of 1, whereas hydrocortisone butyrate, mometasone furoate, and methylprednisolone aceponate are allowed for patients above the age of 2. Other topical GCs may be used above the age of 6 or 12.

Table 4. Age of use topical GCs according to the SPC

Topical GCs	Age from the SPC
Fluticasone propionate	> 1 y/o
Alclometasone	
Betamethasone valerate	
Hydrocortisone butyrate	> 2 y/o
Mometasone furoate	
Methylprednisolone aceponate	

Adverse reactions of preparations containing topical glucocorticosteroids

Long-term use of topical GCs, especially from the groups that have potent effects, is often associated with adverse reactions such as: skin atrophy, permanent vasodilation (telangiectasias), stretch marks, hypertrichosis, dyspigmentation, perioral dermatitis, bacterial and/or fungal superinfections, cataracts, glaucoma, withdrawal effect (exacerbation of skin lesions after drug discontinuation), and tachyphylaxis (gradual decrease in drug efficacy as the drug is used long-term). Paradoxically, a contact allergy may also develop. Topical application of potent topical GCs on large areas in children, and infants in particular, may cause general adverse reactions: inhibition of the hypothalamic-pituitary-adrenal axis, growth failure, and osteoporosis. Fear of adverse reactions is the most common reason for non-observance of physician's recommendation by patients, and in case of children – by their parents, what in turn leads to lack of treatment efficacy. To avoid potential adverse reactions, it is recommended to use a so-called intermittent therapy that is based on using topical GCs only 2–3 days a week and emollients alternately. Topical GCs should be used according to the manufacturer's recommendations, because its frequent use does not increase the treatment efficacy – it rather increases the risk for adverse reactions. Additionally, a FTU (finger tip unit) rule may help in safe application of these drugs [17, 70–73].

Steroid phobia

More than half of AD-patients fear the use of topical GCs, what has been revealed by studies conducted among the patients. Furthermore, it was showed that patients have little knowledge about the therapeutic potential of topical GCs and their adverse reactions, and the main source of knowledge for patients is the Internet. The problem of steroid phobia is not limited to Poland, but regards the entire Europe and is a reason behind inefficacy of topical AD therapies. Proper education of patients and interpersonal relations between patients and physicians that are based on mutual trust, could improve the efficacy of AD treatment [74]. Patients with steroid phobia should be identified and educated by physicians and pharmacists, what might improve observance of recommendations [18].

Topical calcineurin inhibitors

Topical calcineurin inhibitors – tacrolimus and pimecrolimus – inhibit activation of T lymphocytes and release of inflammatory cytokines. Pimecrolimus as a 1% cream is recommended as the first-line treatment in mild AD, and its clinical profile suggested that it may be also considered as a treatment of choice in mild and moderate AD, both in children and adults, especially within sensitive skin regions [75]. Tacrolimus as 0.03% and 0.1% ointment is recommended in moderate and severe atopic eczema. Tacrolimus, as compared with pimecrolimus, shows faster and more potent effects, and clinical improvements after its use are visible already during the first week of treatment. These preparations are applied twice a day till inflammation disappears, with special indication for sensitive skin regions such as bends, face, neck, intertriginous areas, and the skin of genital organs both in adults and children. Patients treated with topical calcineurin inhibitors should have effective sun protection recommended [18]. As opposed to topical GCs, topical calcineurin inhibitors do not inhibit collagen synthesis, do not cause epidermal thinning, vasodilation, and do not damage the skin barrier. The cause neither cataracts nor glaucoma [18]. The most common adverse reaction associated with the use of topical calcineurin inhibitors is connected to neuropeptide release – a burning sensations and skin reddening that usually lasts about 30 min at the site of application and disappears after several days [17, 18, 75, 76].

Based on existing analyses of treatment results, it is believed that limits regarding the use of pimecrolimus in infants are unfounded. It is suggested to prepare new recommendations and warning on labels of topical calcineurin inhibitors [77]. Tacrolimus as a 0.1% ointment has a more potent effect than pimecrolimus as a cream. Topical calcineurin inhibitors show a significant therapeutic effect in long- and short-term treatment of AD [18].

Treatment of acute inflammatory lesions should include topical GCs initially, and then topical calcineurin inhibitors [18]. Topical GCs are also recommended to control pruritus at an initial stage of AD exacerbation; then, until the symptoms disappear – topical calcineurin inhibitors [19]. Polidocanol may be used topically in order to decrease pruritus; furthermore, UVB and UVA1 phototherapy is recommended [18, 19].

Proactive therapy

A proactive therapy is a long-term intermittent therapy involving topical anti-inflammatory preparations used at sites where eczema used to appear, after its remission. Studies involving tacrolimus in proactive therapies lasted up to 12 months. A decrease in frequency of AD exacerbations, extension of the period till the first disease exacerbation, improvement in patients' quality of life, and decrease in AD treatment costs were showed among patients that used proactive therapies with tacrolimus. A proactive therapy used twice a week for a longer period of time may help reduce disease recurrences [18, 78, 79].

Wet dressings

A so-called "wet dressings" therapy may be used in children aged from 6 months to 10 years with severe AD (SCORAD above 50 points). This method uses two layers of dressings: the first wet one is placed directly on

the skin with applied emollient or 0.05% fluticasone propionate or mometasone furoate that is properly diluted (1 : 3, 1 : 9, 1 : 19), and then the second dry layer of a superficial dressing. The therapy lasts from 3 to 14 days and is conducted under strict supervision of a physician, with the use of diluted topical GCs, most often in the hospital, and requires monitoring of the cortisol level in the mornings, because its adverse reaction may include suppression of adrenal glands [80].

Wet dressings have a cooling, anti-inflammatory, and anti-pruritic effects. They create a mechanical barrier against external environmental factors and protect the child from scratching, while potentially decrease the amount of used topical GCs. On the other hand, they cause an increased absorption of topical GCs, risk for developing bacterial infections, and skin atrophy. Moreover, this form of therapy requires training of caretakers or patients, what increases its cost [81].

Treatment by means of "wet dressings" is a safe therapy in severe and recurrent AD cases; it is tolerated well by children and significantly increases their quality of life [82]. Spectacular effects observed already after a week of treatment with this method are highlighted, however, in some cases within 4 weeks from the treatment discontinuation a considerable worsening of AD may occur; hence, studies on proactive application of wet dressings are conducted [82]. Studies' results encourage to use this method, however, further controlled standardized clinical studies are need to recommend it [83].

Antimicrobial treatment

Skin of AD-patients does not have a natural microbiological diversity [84, 85]. During disease exacerbation periods, bacterial flora of AD-patients' skin is dominated by *S. aureus* [85]. Every exacerbation of AD symptoms may be associated with an infection, most often staphylococcal, and eradication of *S. aureus* improves the disease course [86]. Studies indicate therapeutic efficacy of octenidine, chlorhexidine, mupirocin, fusidic acid, and retapamulin against *S. aureus*. Usage of antiseptic baths with addition of sodium hypochlorite decreases the number of bacteria, reduces pruritus, and improves patient's clinical condition [18]. It is not recommended to use topical antibiotics chronically as resistance to antibiotics may develop [18, 19, 86–89]. A justification for the use of oral antibiotics is exacerbation of AD with clinical signs of bacterial infection. In other cases, treatment involving oral antibiotics is not recommended [17–19, 90, 91]. Short cycles of oral antibiotics, e.g. cephalosporin, may be considered in patients with clinical signs of an infection with *S. aureus* [18, 19]. Due to a disordered profile of antibacterial peptides in AD, achieving a continual skin decolonization is practically impossible [88]. Anti-inflammatory treatment (topical calcineurin inhibitors, topical GCs, UV) decrease colonization with *S. aureus* in AD [17].

Atopic skin infection with herpes simplex virus (HSV) often manifests itself as eczema herpeticum (Kaposi varicelliform eruption; eczema herpetiformis – EH) and requires immediate systemic antiviral treatment with acyclovir [18, 92]. AD-patients with lesions found on the head, face, and neck, also suffer from concomitant infection with yeasts – *Malassezia* sp., which disappears after the use of topical antifungal treatment (ketoconazole or ciclopirox olamine) [18, 93–95].

Phototherapy

Phototherapy may be used as monotherapy or in combination with topical GCs (Table 5). Narrow-band UVB (NB-UVB – 311 nm) is an effective and safe method in the treatment of moderate and severe AD in school children and adults [96]. Furthermore, moderate doses of UVA1 (340–400 nm) are recommended for adults with AD; PUVA may be used in selected cases [18, 19, 97, 98]. A limitation of phototherapy is its little availability. Rare adverse reactions include: erythema and tenderness after radiation, pruritus, burns and post-sun skin damage, skin cancers, melanoma, lentigines, photosensitivity reactions (mainly polymorphous light eruptions), folliculitis, photoonycholysis, HSV reactivation, excessive facial hair growth, and cataracts [97].

Conflict of interest

The authors declare no conflict of interest.

Table 5. Phototherapy in AD [96, 97]

Narrow-band UVB (NB-UVB)	Initiating dose for phototype I: 130 mJ/cm^2, II: 220 mJ/cm^2, III: 260 mJ/cm^2, IV: 330 mJ/cm^2, V: 350 mJ/cm^2, VI: 400 mJ/cm^2. With every radiation the dose is increased for phototype I with 15 mJ/cm^2 (max. dose 2000 mJ/cm^2), II – with 25 mJ/cm^2 (max. dose 2000 mJ/cm^2), III – with 40 mJ/cm^2 (max. dose 3000 mJ/cm^2), IV – with 45 mJ/cm^2 (max. dose 3000 mJ/cm^2), V – with 60 mJ/cm^2 (max. dose 5000 mJ/cm^2), VI – with 65 mJ/cm^2 (max. dose 3000 mJ/cm^2). Subsequent doses 3–5 times. In case 1 week of radiation is missed – the last dose may be maintained; 2 weeks – decrease the dose by 25%; 3 weeks – decrease the dose by 50%; 4 weeks – start from the beginning
Adjuvant therapy NB-UVB method	Disappearance of lesions > 95%: last dose once/week for 4 weeks, then 1 dose decreased by 25% every 2 weeks – for 4 weeks, then once/month 50% of the highest dose

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